

The Nitration of Carbamates Using Boron
Trifluoride as a Dehydrating Agent

by

Guy Herbert Wayne, Jr.

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Thesis

THE NITRATION OF CARBAMATES USING
BORON TRIFLUORIDE AS A DEHYDRATING AGENT

by

Guy Herbert Wayne, Jr.
(A.B., DePauw University, 1945)

submitted in partial fulfilment of the
requirements for the degree of
Master of Arts
1947

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THE NITRATION OF CARBAMATES USING BORON TRIFLUORIDE AS A DEHYDRATING AGENT

I. INTRODUCTION

A. Historical Survey

1. Preparation of Nitro Carbamates

The research involving the nitration of the carbamates has been very insignificant compared to that conducted on other organic reactions. The majority of the investigations were made prior to the twentieth century by Franchimont, Klobbie, Thomas and Van Erp (5,6,15,18). The primary interest was not in the nitro carbamates but in the product produced by their ammonolysis, the N-nitro amino alkanes. In most cases the wet ethereal extract of the nitration reaction was merely treated with a steady stream of ammonia without isolating the nitro carbamate. Since there was no need of obtaining the pure intermediate, the physical constants of these compounds were found to be lacking in both quantity and quality. In the few cases where the nitro carbamates had been isolated the majority of the attempts to purify them by distillation had resulted in explosions, yet none of the investigators apparently tried distillations under reduced pressure. (Such a method was known for it had been used by others even at this early date.) This also might explain why the reported physical constants were always taken on the impure product in those few cases where the nitro carbamate was isolated.

The four men, over a period of about ten years, prepared a total of seventeen nitro carbamates (either as intermediates

or end products) and reported the boiling points (if distillation were possible at atmospheric pressure), the refractive indexes and the specific gravities of the crude materials. Each man used a slightly different method of preparation and their methods are reported in the following section without regard to the specific quantities of starting reagents that were used.

The aim of my research was to collect and correlate the previous work and investigate other possible methods of nitration.

Late in the nineteenth century Franchimont and Klobbie (5) prepared the first nitro carbamate, ethyl-N-nitro-N-ethyl carbamate, as an intermediate in the synthesis of N-nitro aminoethane. The nitration was accomplished by treating the carbamate with absolute nitric acid, pouring the reaction mixture into water and extracting the oil with ether. At the same time, these investigators also nitrated ethyl-N-methyl carbamate and two dicarbamates, ethylene di-(methyl carbamate) and pentylene di-(methyl carbamate).

The following year, several of the ethyl-N-nitro-N-alkyl carbamates and methyl-N-nitro-N-alkyl carbamates were prepared (6) by allowing ethyl chloroformate or methyl chloroformate to react with the potassium salt of the N-nitro amino alkane in an aqueous medium and extracting the oil formed with ether.

Thomas (15) reported 80-90% nitration of ethyl-N-propyl

carbamate and methyl-N-propyl carbamate when the organic compound was added dropwise to 100% nitric acid while the reaction mixture was cooled in a water bath. The reaction mixture after standing, was poured onto sodium carbonate crystals and then extracted with ether. More difficulty was experienced with the isopropyl isomer. Nitration, without excessive oxidation, was possible only when the reactions were carried out in a similar manner but at temperatures below 0°C. This unusual reactivity was attributed by Thomas to the single hydrogen on the central carbon of the isopropyl group.

In 1895 Van Erp (18) prepared the isomers of ethyl-N-nitro-N-butyl carbamate and methyl-N-nitro-N-butyl carbamate and also ethyl-N-nitro-N-hexyl carbamate. One mole of the n-butyl or the isobutyl isomer was added dropwise to 4-5 moles of absolute nitric acid at 0°C. The reaction mixture, after standing, was poured slowly into a sodium carbonate -- ice mixture, and the oil that separated was extracted with ether. Oxidation occurred much more readily with the sec-butyl isomer. In order to obtain a fair yield the reaction had to be carried out with eight moles of absolute nitric acid at -18°C. The ethyl-N-hexyl carbamate was nitrated with four moles of absolute nitric acid while the reaction mixture was cooled merely in a water bath.

Van Erp also attempted the nitration of ethyl-N-butyl carbamate using the calculated amount of concentrated sulfuric acid and nitric acid (sp. gr. 1.485), but even after

carbamate and methyl-n-propyl carbamate when the organic compound was added dropwise to 100% nitric acid while the reaction mixture was cooled in a water bath. The reaction mixture after standing, was poured onto sodium carbonate crystals and then extracted with ether. More difficulty was experienced with the isopropyl isomer. Extraction, without excessive oxidation, was possible only when the reactions were carried out in a similar manner but at temperatures below 0°C. This unusual reactivity was attributed by Thomas to the alpha hydrogen on the central carbon of the isopropyl group.

In 1895 Van Eyr (18) prepared the isomers of ethyl-n-nitro-n-butyl carbamate and methyl-n-nitro-n-butyl carbamate and also ethyl-n-nitro-n-hexyl carbamate. One mole of the n-butyl or the isobutyl isomer was added dropwise to 4-5 moles of absolute nitric acid at 0°C. The reaction mixture, after standing, was poured slowly into a sodium carbonate -- ice mixture, and the oil that separated was extracted with ether. Oxidation occurred much more readily with the n-butyl isomer. In order to obtain a fair yield the reaction had to be carried out with eight moles of absolute nitric acid at -18°C. The ethyl-n-hexyl carbamate was nitrated with four moles of absolute nitric acid while the reaction mixture was cooled merely in a water bath.

Van Eyr also attempted the nitration of ethyl-n-butyl carbamate using the calculated amount of concentrated sulfuric acid and nitric acid (sp. gr. 1.485), but even after

prolonged contact at 0°C. no nitrated carbamate was recovered (18). Later attempts along this line proved more successful but the reactions were difficult to control. In 1944-45 Dr. J.P. Mason (10), of this laboratory, nitrated methyl-N-isopropyl carbamate and methyl-N-n-butyl carbamate with a five fold excess of fuming nitric acid and concentrated sulfuric acid at 0-5°C. Again the most difficult nitration was that of the isopropyl carbamate. This fact seemed to further substantiate Thomas's theory regarding the isopropyl group's easily oxidizable structure.

Thiele and Lachmann (14), contemporaries of Van Erp, nitrated ethyl carbamate, a solid, by dissolving it in concentrated sulfuric acid and cooling the solution to 0°C. Ethyl nitrate was added slowly keeping the temperature at -5°C. Forty-five minutes after the addition was completed the reaction mixture was poured into about two kilograms of ice and the oil that separated was extracted with ether.

The experiments of Dr. Richard Bailes (1), of this laboratory, in 1944-45, revealed that it was possible to nitrate the carbamates with fuming nitric acid when a large excess was used. When the carbamate was added to an eight to ten fold excess of the acid at 0-5°C. a fairly good yield of the following N-nitro-O-methyl carbamates was obtained, N-methyl, N-ethyl, N-propyl, N-n-butyl, N-isobutyl, N-sec-butyl, and N-heptyl. It was found in the preparation of methyl-N-nitro-N-isopropyl carbamate that oxidation accompanied the nitration

proposed contact at 0°C. no nitrated carbenate was recovered (18). Later attempts along this line proved more successful but the reactions were difficult to control. In 1944-45 Dr. J.P. Hansen (19), of this laboratory, nitrated methyl-N-isopropyl carbenate and methyl-N-n-butyl carbenate with a five fold excess of fuming nitric acid and concentrated sulfuric acid at 0-5°C. Again the most difficult nitration was that of the isopropyl carbenate. This fact seemed to further substantiate Hansen's theory regarding the isopropyl group's easily oxidizable structure.

Thiele and Lachmann (14), contemporaries of Van Wazer, nitrated ethyl carbenate, a solid, by dissolving it in concentrated sulfuric acid and adding the solution to 0°C. Ethyl nitrate was added slowly keeping the temperature at -5°C. Forty-five minutes after the addition was completed the reaction mixture was poured into about two kilograms of ice and the oil that separated was extracted with ether.

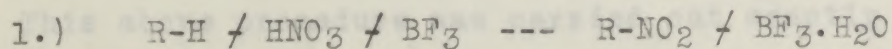
The experiments of Dr. Richard Bates (1), of this laboratory, in 1944-45, revealed that it was possible to nitrate the carbenates with fuming nitric acid when a large excess was used. When the carbenate was added to an eight to ten fold excess of the acid at 0-5°C. a fairly good yield of the following N-nitro-N-methyl carbenates was obtained, N-methyl, N-ethyl, N-propyl, N-n-butyl, N-isobutyl, N-sec-butyl, and N-tert-butyl. It was found in the preparation of methyl-N-nitro-N-isopropyl carbenate that oxidation accompanied the nitration

unless the reaction was conducted at very low temperatures.

It has been found (3), however, that the carbamates are nitrated most efficiently when fuming nitric acid (50% excess) was added to acetic anhydride at 10°C. and this mixture used as the nitrating agent. The carbamate was then slowly added to the acidic solution while the temperature was kept below 20°C. On completion, the reaction mixture was poured into two to three times its volume of water. The oil that settled to the bottom was extracted with ether, dried with potassium carbonate and distilled.

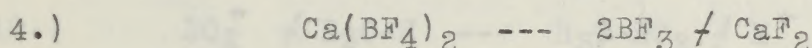
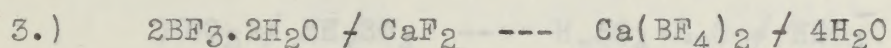
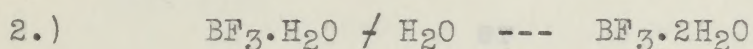
2. Nitrations using Boron Trifluoride

A recent article by Thomas, Anzilotti and Hennion, (16), of Notre Dame, on the nitration and sulfonation of negatively substituted benzenes at temperatures below 100°C., when boron trifluoride was used as a dehydrating agent, suggested the possibility of applying this method of nitration to the nitration of carbamates. During the last fifteen years the Department of Chemistry at Notre Dame has conducted a wide survey of the uses of boron trifluoride as an acid catalyst in organic replacement reactions. The experiments on nitration and sulfonation revealed that boron trifluoride was an excellent catalyst for substitution reactions where water was one of the products. The mono-hydrate ($\text{BF}_3 \cdot \text{H}_2\text{O}$) was formed, thereby removing one of the products and shifting the reaction toward completion.



Further investigation showed that the boron trifluoride

could be recovered by the following method: the reaction mixture was treated with only an additional equivalent of water; the boron trifluoride dihydrate ($\text{BF}_3 \cdot 2\text{H}_2\text{O}$) formed was distilled under reduced pressure; the dihydrate was then allowed to react with an excess of calcium fluoride to form calcium fluoborate; upon heating this compound liberated boron trifluoride. (16)

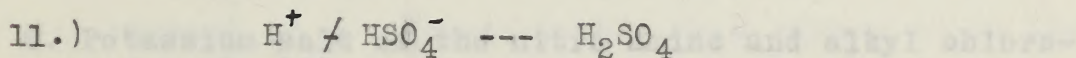
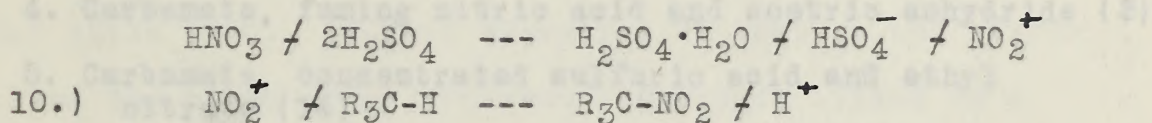
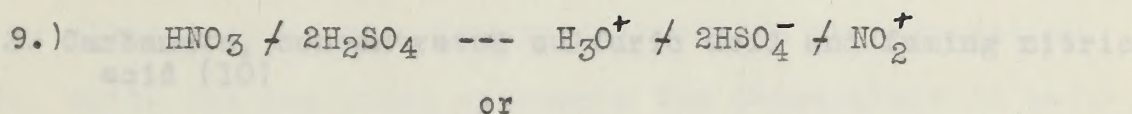


The ability to recover the catalyst for reuse made this synthesis commercially feasible. Shortly after this work was reported in the literature, G.A.Hennion (for E.I.DuPont de Nemours and Company) was granted a patent (8) covering an identical procedure for preparing nitrobenzenes.

A typical reaction in the original paper (16) was the nitration of nitrobenzene to m-dinitrobenzene. To 31 g. (0.25 mole) of nitrobenzene was added 20.2 g. (0.3 mole) of fuming nitric acid. Boron trifluoride was admitted with stirring until 17 g. (0.25 mole) was absorbed while the reaction temperature was kept below 80°C . The temperature was then raised to 100°C . and kept there for one-half hour. The reaction mixture was then poured into 500 cc. of hot water. After standing, the solid dinitrobenzene was filtered off. Yield 36.7 g. (87%)

This above procedure was carried out exactly as described. The reaction went smoothly, without decomposition or oxidation

regarded as the criterion of excellent yields.) This fact, along with several others, indicated that the first step was not a simple ionization and that the so called "dehydration reaction" (equation 8) does not occur in the reaction. Their mechanism was as follows:



If the two theories are compared, it will be noted that both account for some method of dehydration, the former at the end of the reaction and the latter at the beginning. But, as stated above, the mechanism outlined by Karasch is not of the type that is usually thought of when dehydration is involved. (The reaction, as shown in equation 8, is the usual type.)

The investigation of the various dehydrating agents that could best accomplish this constituted the scope of this research. Such a dehydrating agent was of paramount interest because then it would be possible to effect complete nitration with only an equivalent, or slightly more, of nitric acid.

1. Suggested Method of Approach

The use of boron trifluoride usually decreased the amount of acid necessary and also the reaction temperature. On the other hand, its use increased the rate of the reaction and the

B. Outline of Problem

Thus far, six basic methods have been used for the preparation of nitro carbamates, namely:

1. Carbamate and absolute nitric acid (5,18)
2. Carbamate and fuming nitric acid (1)
3. Carbamate, concentrated sulfuric acid and fuming nitric acid (10)
4. Carbamate, fuming nitric acid and acetic anhydride (3)
5. Carbamate, concentrated sulfuric acid and ethyl nitrate (14)
6. Potassium salt of the nitro amine and alkyl chloroformate (6)

All of the preparations involving nitric acid (except the fourth one) required at least four or five times the theoretical amounts. This excess acid provided a high concentration of nitroxyl cations upon which the extent of the nitration was dependent. It should be possible to obtain the same effect by removing the water that is formed during the reaction and the majority of the water that is present in the nitric acid employed. The investigation of the various dehydrating agents that could best accomplish this constituted the scope of this research. Such a dehydrating agent was of paramount interest because then it would be possible to effect complete nitration with only an equivalent, or slightly more, of nitric acid.

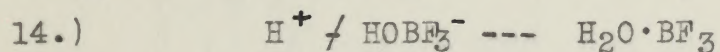
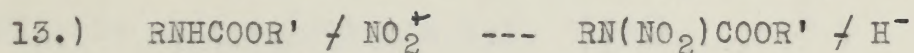
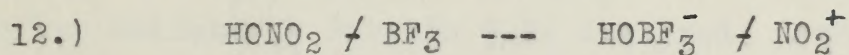
1. Suggested Method of Approach

The use of boron trifluoride usually decreased the amount of acid necessary and also the reaction temperature. On the other hand, its use increased the rate of the reaction and the

purity of the product. These were the very features desired in the preparation of the nitro carbamates. ~~reaction that occurs.~~

The reaction of substituted alkyl carbamates with nitric acid is similar to that of nitrobenzene in many respects, the main difference being the temperature at which the reagents are usually allowed to react. The dinitrobenzene is prepared at 100°C., while for the nitro carbamate the temperature is maintained below 100°C. Another exception is that in the latter reaction the nitro group replaces a hydrogen linked to a nitrogen instead of a hydrogen linked to a carbon as in the former case. It was therefore thought possible to apply this method of synthesis to that of nitro carbamates.

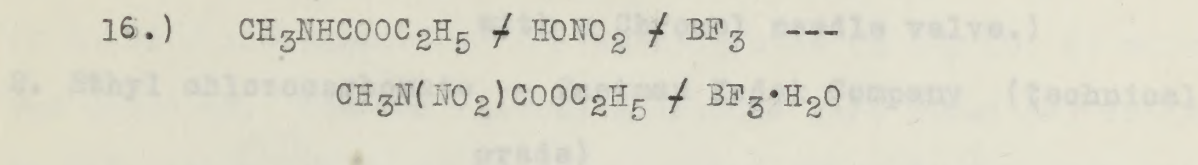
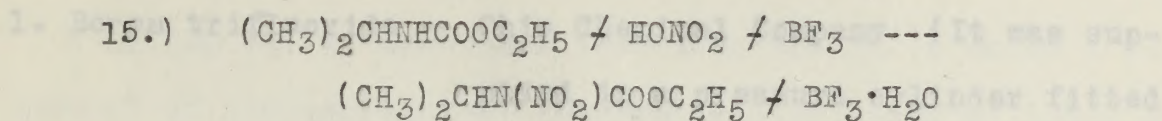
When boron trifluoride is used as a dehydrating agent in the nitration of a carbamate, a reaction mechanism similar to that of Westheimer and Kharasch (17) might be predicted.



In light of the theory it would be incorrect to refer boron trifluoride as strictly a dehydrating agent, but for all practical purposes that is its net effect.

Two series of nitrations were performed. Ethyl-N-isopropyl carbamate was used in the beginning because the isopropyl amine used to prepare the carbamate was the most readily obtainable of the low molecular weight amines. When it was found that the ethyl-N-isopropyl carbamate was easily oxidized under the

reaction conditions, ethyl-N-methyl carbamate was substituted. The following equations indicate the net reaction that occurs.



3. Isopropylamine -- Commercial Solvents Company (100%)

4. Methylamine hydrochloride -- Eastman Kodak Company (tech-
nical grade)

5. Nitric acid (fuming) -- Baker's C.P. Analyzed (89-95%)

Specific gravity 1.49-1.50;

Lot number 111,714

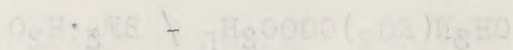
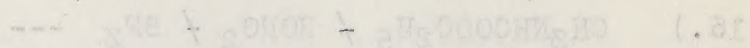
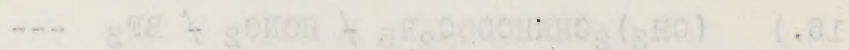
6. Potassium carbonate -- Baker's C.P. Analyzed (anhydrous)

7. Sodium nitrate -- Baker's C.P. Analyzed

8. Sodium sulfate -- Baker's C.P. Analyzed (anhydrous)

9. Sulfuric acid -- Baker's C.P. (98%)

reaction conditions, ethyl-*N*-methyl carbamate was substituted. The following equations illustrate the net reaction that occurs.



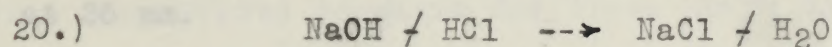
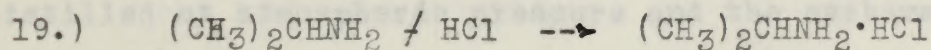
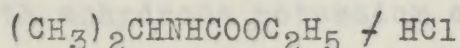
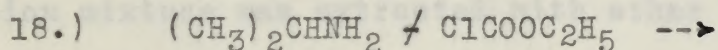
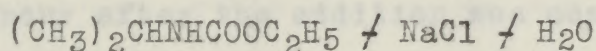
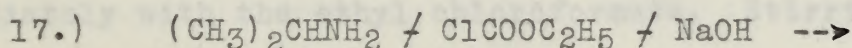
C. Standard Commercial Reagents Used

Reagent	Source and Description
1. Boron trifluoride	-- Ohio Chemical Company (It was supplied in a pressure cylinder fitted with a Chromel needle valve.)
2. Ethyl chlorocarbonate	-- Eastman Kodak Company (technical grade)
3. Isopropylamine	-- Commercial Solvents Company (100%)
4. Methylamine hydrochloride	-- Eastman Kodak Company (technical grade)
5. Nitric acid (fuming)	-- Baker's C.P. Analyzed (89-95%) Specific gravity 1.49-1.50; Lot number 111,714
6. Potassium carbonate	-- Baker's C.P. Analyzed (anhydrous)
7. Sodium nitrate	-- Baker's C.P. Analyzed
8. Sodium sulfate	-- Baker's C.P. Analyzed (anhydrous)
9. Sulfuric acid	-- Baker's C.P. (98%)

D. Preparation of the Carbamates

1. Ethyl-N-isopropyl Carbamate

In 120 cc. of water was dissolved 252 g. (4 moles \nearrow 5% excess) of isopropylamine. Meanwhile a solution of 195.4 g. (4 moles \nearrow 10% excess) of sodium hydroxide in 500 cc. of water was prepared. The two aqueous solutions were mixed and cooled to 0°C. Then 482 g. (4 moles) of ethyl chloroformate was added dropwise keeping the reaction mixture below 10°C. with an ice-salt bath. Stirring was continued for a half-hour after the addition was completed. The reaction mixture was placed in a separatory funnel and the bottom layer drawn off. The top layer was dried over the minimum of potassium carbonate until the oil was clear. The oil was filtered and distilled under reduced pressure, using a water aspirator. B.P. 88-92°C. at 25 mm.



The sodium hydroxide was provided to neutralize (equation 20) the hydrogen chloride as it formed (equation 18). If the hydrogen chloride were not removed, it would have reacted with an equivalent of the isopropylamine forming the salt (equation 19). This would have prevented part of the amine from reacting with the ethyl chloroformate.

2. Ethyl-N-methyl Carbamate

The procedure was similar to that above except that methylammonium chloride was used. Therefore an additional equivalent of sodium hydroxide was needed. Sixty-seven grams (1.03 moles) of methylammonium chloride was dissolved in 30 cc. of water containing a few drops of phenolphthalein and cooled to 0°C. A solution of 82 g. (2.05 moles) of sodium hydroxide* in 200 cc. of water and 108 g. (1 mole) of ethyl chloroformate were added simultaneously with rapid stirring to the amine salt solution. The reaction was carried out at 0-10°C. and was kept slightly basic all the time. If all the base were added at the beginning of the reaction the amine which is a gas would be liberated and therefore escape. By keeping the reaction mixture just barely basic only enough free amine is present to react immediately with the ethyl chloroformate. Stirring was continued for a half-hour after the addition was completed. The reaction mixture was extracted with ether and the ethereal solution was dried with anhydrous potassium carbonate. The ether was distilled at atmospheric pressure and the carbamate at 87°C. at 35 mm.

*In this reaction one mole of sodium hydroxide was necessary to liberate the amine from its salt. The second mole served to neutralize the hydrogen chloride formed in the reaction.

II. NITRATION OF ETHYL-N-ISOPROPYL CARBAMATE

A. Nitration with fuming Nitric Acid

The only data regarding the nitrating strength of fuming nitric acid alone toward the carbamates available was the work of R. Bailes (1). In all these experiments a large excess of acid had been used in order to secure adequate nitration. Since the main interest of this present work was the extent of nitration produced in a reaction where only an equivalent (plus a slight excess) of acid was used, it was necessary to conduct a controlled experiment of this nature.

To 21.8 g. (0.17 mole) of ethyl-N-isopropyl carbamate was added slowly 14.7 g. (0.17 mole / 20% excess) of fuming nitric acid. The temperature was kept between 55°C. and 70°C. by occasional heating with a steam bath. This elevated temperature was used in order to insure complete reaction even at the expense of oxidation. The reaction was not very exothermic and not until about half of the acid had been added was there any sign of oxidation. At this point the reaction began to turn yellow and nitrogen dioxide was slowly evolved. The acid mixture was allowed to stand for three hours after the addition had been completed, and then a portion of it was poured into water. The oil rose to the surface, indicating that no nitro carbamate had been formed. The remainder of the reaction mixture was allowed to stand overnight and then diluted with a large quantity of water. An oil sank to the bottom, which seemed to indicate that the oil was the nitro carbamate.

However, when the aqueous solution was shaken vigorously and permitted to stand another day, the oil rose to the surface. Evidently the nitric acid absorbed by the carbamate gave the oil a specific gravity greater than one. Not until this acid was washed free did the carbamate exhibit its true density.

In both cases, where the reaction was allowed to stand for three hours and where it was allowed to stand overnight, there was apparently no nitration.

B. Nitration with fuming Nitric Acid and concentrated Sulfuric Acid

A nitric acid-sulfuric acid mixture similar to that of Van Erp's (17) was used in the next attempted nitration. Although this mixture has been employed by this department in successful nitrations at 0°C. (10), it was desirable to determine what effect a higher temperature would have on the reaction.

The mixing of 12 g. (0.17 mole \neq 50% excess) of fuming nitric acid and 12 cc. (equal volume by weight) of concentrated sulfuric acid was quite exothermic. This was probably due to hydration of the sulfuric acid by the 13% water present in the nitric acid. The mixed acid was cooled to room temperature and added dropwise to 21.7 g. (0.17 mole) of ethyl-N-isopropyl carbamate at 25-40°C. The reaction temperature varied directly with the rate of the acid's addition but there was a "reaction lag". About two-thirds of the acid was added before oxidation started. The stirring was stopped and the addition was immediately discontinued. The liquid in the flask began to boil and evolve nitrogen dioxide. When the temperature reached 100°C., the majority of the material "bumped" out of the flask. The residue that was left was soluble in water and smelled like nail-polish. This experiment proved that nitration with mixed acids was impossible at elevated temperatures without oxidation.

B. Nitration with Fuming Nitric Acid and concentrated Sulfuric Acid

A nitric acid-sulfuric acid mixture similar to that of Van Ryp's (17) was used in the next attempted nitration. Although this mixture has been employed by this department in successful nitrations at 0°C. (10), it was desirable to determine what effect a higher temperature would have on the reaction.

The mixing of 12 g. (0.17 mole) of fuming nitric acid and 12 cc. (equal volume by weight) of concentrated sulfuric acid was quite exothermic. This was probably due to hydration of the sulfuric acid by the 15% water present in the nitric acid. The mixed acid was cooled to room temperature and added dropwise to 21.7 g. (0.17 mole) of ethyl-*n*-isopropyl carboxylate at 25-40°C. The reaction temperature varied directly with the rate of the acid's addition but there was a "reaction lag". About two-thirds of the acid was added before oxidation started. The stirring was stopped and the addition was immediately discontinued. The liquid in the flask began to boil and evolve nitrogen dioxide. When the temperature reached 100°C., the majority of the material "bumped" out of the flask. The residue that was left was soluble in water and smelled like nail-polish. This experiment proved that nitration with mixed acids was impossible at elevated temperatures without oxidation.

C. Nitration with fuming Nitric Acid and Boron Trifluoride

1. Solubility of Boron Trifluoride in Ethyl-N-isopropyl Carbamate

The boron trifluoride was passed through a tube, with a capillary tip, into 32.7 g. of ethyl-N-isopropyl carbamate in an Erlenmeyer flask fitted with a three-hole rubber stopper containing a thermometer, vent tube and the addition capillary.

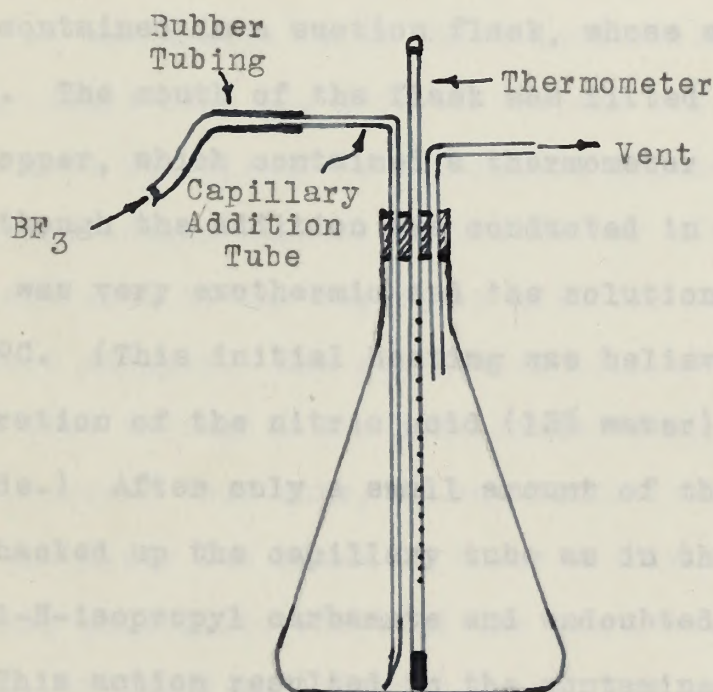


Figure 1

Only about 4 g. of the boron trifluoride was added at 0-5°C. before the carbamate was drawn up the capillary tube into the rubber tubing connecting it to the needle valve by a slight vacuum created by the absorption of boron trifluoride in the carbamate more rapidly than the gas was being supplied. When the carbamate was forced back into the flask by increasing

C. Nitration with Fuming Nitric Acid and Boron Trifluoride

1. Solubility of Boron Trifluoride in Ethyl-N-isopropyl Carbamate

The boron trifluoride was passed through a tube, with a capillary tip, into 52.5 g. of ethyl-N-isopropyl carbamate in an Erlenmeyer flask fitted with a three-hole rubber stopper containing a thermometer, vent tube and the addition capillary.

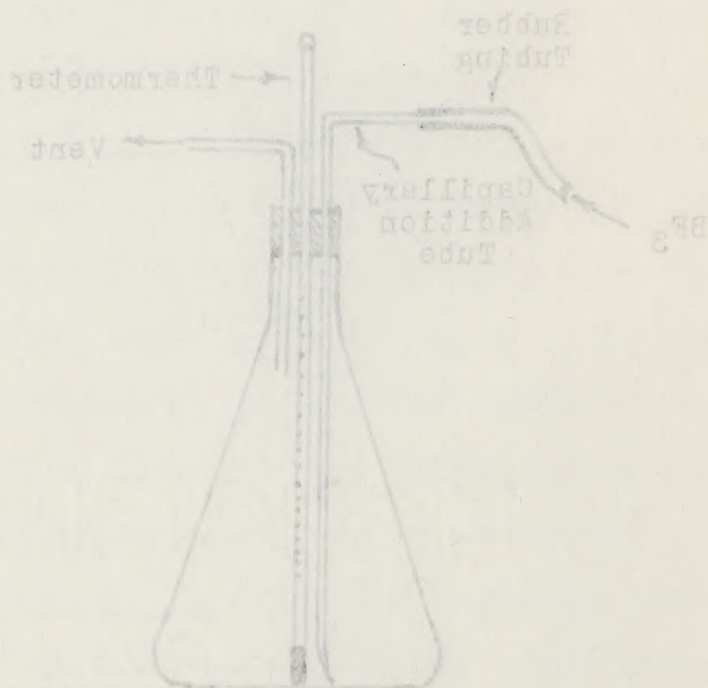


Figure 1

Only about 4 g. of the boron trifluoride was added at 0-5°C. before the carbamate was drawn up the capillary tube into the rubber tubing connecting it to the needle valve by a slight vacuum created by the absorption of boron trifluoride in the carbamate more rapidly than the gas was being supplied. When the carbamate was forced back into the flask by increasing

the gas pressure it was found to be discolored. The contamination was due to a reaction with the rubber tubing. The boron trifluoride seemed to be only slightly soluble in the carbamate because it came out of the solution almost as fast as it was added.

2. Solubility of Boron Trifluoride in Nitric Acid

The boron trifluoride was again passed through a tube, with a capillary tip, into 22 g. of fuming nitric acid. The acid was contained in a suction flask, whose side-arm served as a vent. The mouth of the flask was fitted with a two-hole rubber stopper, which contained a thermometer and the addition tube. Although the addition was conducted in an ice bath the solvation was very exothermic and the solution could not be kept at 0°C. (This initial heating was believed to be due to the dehydration of the nitric acid (13% water) by the boron trifluoride.) After only a small amount of the gas was added the acid backed up the capillary tube as in the experiment with ethyl-N-isopropyl carbamate and undoubtedly for the same reason. This action resulted in the contamination of the acid by a reaction with the rubber. A second and third attempt netted identical results. A somewhat hit or miss method was followed in subsequent tests until a procedure was found whereby the desired amount of boron trifluoride could be added quickly without the acid being lost or contaminated.

A 100-cc. bottle was inserted between the needle valve of the boron trifluoride tank and the capillary tube which was now

connected to the bottle by a single piece of glass tubing. (This prevented the acid from coming in contact with any rubber even though it backed up.) The bottle acted as a pressure dome as well as a trap. It was also noted that whenever the rate of addition was decreased or stopped entirely the boron trifluoride was dissolved more rapidly than it was being supplied thereby forming a partial vacuum which sucked the acid back up the capillary. This trouble was alleviated by disconnecting the rubber tubing at the needle valve which equalized the interior and exterior pressure when the rate of the gas flow was reduced. The nitric acid was placed in a 3-necked 500-cc. flask fitted with a mercury sealed stirrer in the center neck. One side neck gave entrance to the capillary addition tube through a one-hole cork stopper. The other neck admitted a thermometer and a vent tube through a two-hole rubber stopper.

After several test runs, it was found that during the addition of the first few grams of boron trifluoride the solvation was very exothermic and that the temperature could only be kept at 0°C . by using an ice-salt bath. The remainder of the gas was added without any further rise in temperature. This further substantiated the preceding conclusion (see the preceding page) that the initial exothermic character of this solution was due to the dehydration of the nitric acid, which contained 13% water, by the boron trifluoride.

The amount of boron trifluoride that had been added was easily determined by weighing the flask containing the acid

before and after the gas had been added. The difference in the two values gave the weight of the gas absorbed.

Reagent	Mole Equivalent	Moles Used	Grams Used
Ethyl-3-isopropyl carbamate	0.25	0.25	32.75
Nitric acid (87%) (20% excess)	0.25 <u>0.03</u>	0.30	22.00
Water present in acid (13%)	0.16		2.86
Boron trifluoride (20% excess) (to dehydrate acid)	0.25 0.03 <u>0.15</u>	0.46	35.2

Twenty-two grams of fuming nitric acid was cooled to 0°C. with an ice-salt bath and 35 g. of boron trifluoride was added at 0-5°C. When all the gas had been absorbed, the solution was brown and contained a drop of mercury which had overflowed from the stirrer. While the reaction was kept below 7°C., 32.7 g. of ethyl-3-isopropyl carbamate was added dropwise. After the addition of the carbamate had been completed, 22 cc. of water was poured into the reaction mixture in order to convert the boron trifluoride monohydrate that was formed to the dihydrate. When about half of the water had been added there was violent foaming due to the evolution of heavy brown fumes (probably nitrogen dioxide and some unreacted boron trifluoride). The foaming was so vigorous that only a trace of the reaction mixture remained in the flask. Also accompanying the foaming was

3. Nitration with the Attempted Recovery of Boron Trifluoride

Table I

Reagent	Mole Equivalent	Moles Used	Grams Used
Ethyl-N-isopropyl carbamate	0.25	0.25	32.75
Nitric acid (87%) (20% excess)	0.25 <u>0.05</u>	0.30	22.00
Water present in acid (13%)	0.15		2.86
Boron trifluoride (20% excess) (to dehydrate acid)	0.25 0.05 <u>0.15</u>	0.45	28.9

Twenty-two grams of fuming nitric acid was cooled to 0°C. with an ice-salt bath and 35 g. of boron trifluoride was added at 0-5°C. When all the gas had been absorbed, the solution was brown and contained a drop of mercury which had overflowed from the stirrer. While the reaction was kept below 7°C., 32.7 g. of ethyl-N-isopropyl carbamate was added dropwise. After the addition of the carbamate had been completed, 29 cc. of water was poured into the reaction mixture in order to convert the boron trifluoride monohydrate that was formed to the dihydrate. When about half of the water had been added there was violent foaming due to the evolution of heavy brown fumes (probably nitrogen dioxide and some unused boron trifluoride). The foaming was so vigorous that only a trace of the reaction mixture remained in the flask. Also accompanying the foaming was

a slight explosion, which was undoubtedly due to the lack of an adequate escape passage for the released gases.

When the previous experiment was repeated, the nitric acid was milky white after the gas had been added. (Evidently the discoloration noted at this point in the preceding experiment was due to contamination by the mercury.) This time the water was added dropwise. The first 5 cc. was added without trouble but during the next twenty drops the reaction mixture began to heat up, followed by foaming and the evolution of nitrogen dioxide.

The same procedure with an even slower addition of the water resulted in a similar oxidation. This time, however, it was possible to add more water before the decomposition occurred by keeping the reaction mixture in an ice-salt bath.

A recalculation of the amount of water necessary to form the dihydrate showed that it should have been only 8 cc. instead of 29 cc. of water. It was assumed that the heat from the formation of the dihydrate from the monohydrate in the secondary reaction was enough to start the oxidation of the organic compounds. (Later work showed that fuming nitric acid alone would decompose the nitro carbamate at room temperature after a few minutes contact.) (3)

No further attempts were made to control the conversion of boron trifluoride from the monohydrate to the dihydrate and its subsequent recovery. Therefore, the emphasis was placed on isolating the nitro carbamate before it was decomposed.

4. Nitration without the Recovery of Boron Trifluoride

a. Addition of the Reaction Mixture to a Large Volume of Ice Water

Approximately 29 g. of boron trifluoride was absorbed in 22 g. of fuming nitric acid at 0-10°C., forming a milky white solution. To this was added dropwise 32.7 g. of ethyl-N-isopropyl carbamate while the reaction mixture was kept below 0°C. This white sirupy mixture was then poured very slowly into 250 cc. of water containing 250 g. of ice. Heavy white fumes were evolved and most of the ice melted, thereby indicating an exothermic solvation. An oil slowly settled to the bottom of the aqueous solution. (This nitro carbamate is heavier than water while the carbamate itself has a specific gravity of less than one.) On this basis it was presumed that the ethyl-N-nitro-N-isopropyl carbamate had been prepared.

The remainder of the experiments were conducted with an apparatus arrangement such as that shown on the following page.

b. Neutralization with Calcium
Hydroxide

The preceding experiment proved that nitration could be accomplished when boron trifluoride was used as a dehydrating agent and that the unused nitric acid, unless diluted, undoubtedly decomposed the products. Therefore, if immediate dilution decreased oxidation, it was believed that neutralization of the acid would have the same effect. The following procedure was used to test that conclusion.

Approximately 23 g. of boron trifluoride was absorbed in 22 g. of fuming nitric acid below 10°C . To this was added 22 g. of ethyl-N-isopropyl carbamate keeping the temperature below 5°C . Then the addition of 10.5 g. of calcium hydroxide (the calculated amount necessary to neutralize the excess acid present) was started in 0.2 g. portions. The neutralization was very exothermic and the reaction mixture foamed out of the flask after only 5.5 g. of the hydroxide had been added. Evidently the neutralization had warmed the reaction mixture sufficiently to allow oxidation to commence.

The remainder of the experiments were conducted with an apparatus arrangement such as that shown on the following page.

A. Variable-speed stirrer

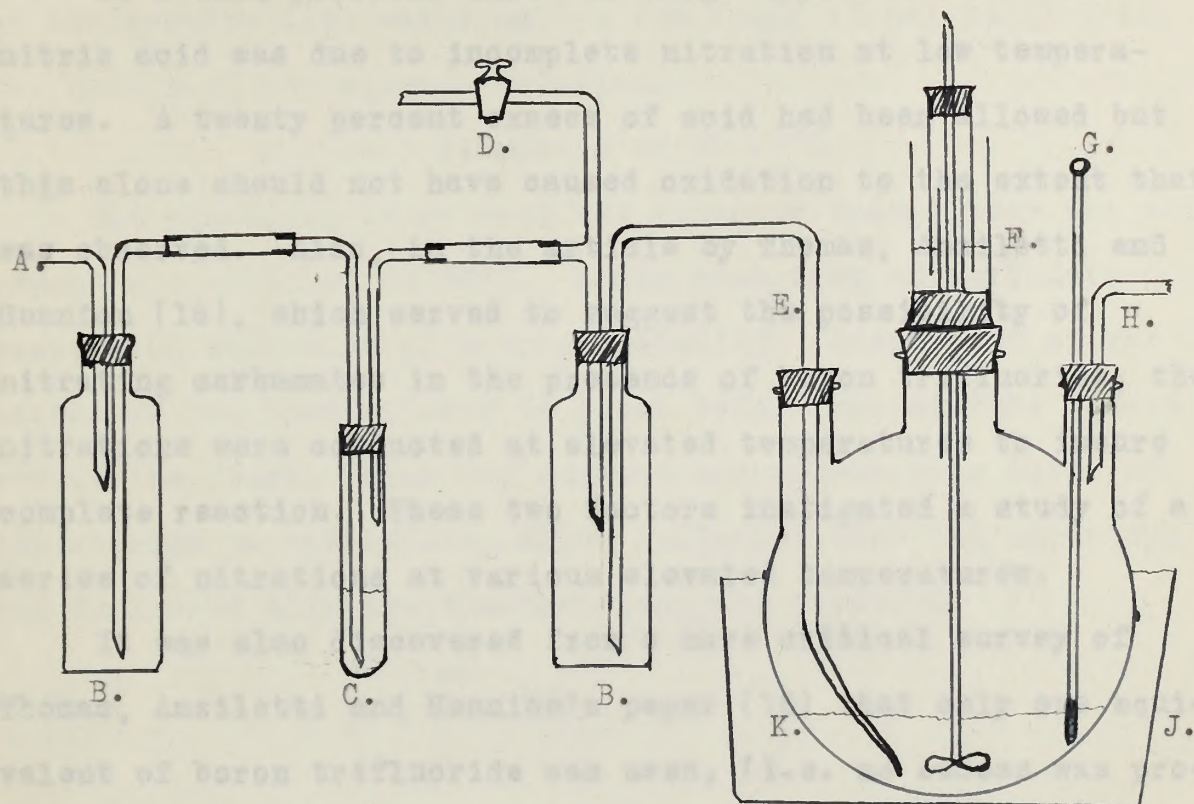
B. Thermometer (-50 to 50°C .)

C. Vent tube

D. Water, Ice or Ice-salt Bath

E. Three-neck, 500-cc. Flask

Figure 2



A. Source of Boron Trifluoride

B. Bottle Traps

C. Test tube -- half filled with paraffin oil (to judge rate of boron trifluoride addition)

D. Stopcock -- to equalize pressure in system when boron trifluoride addition is stopped

E. Capillary Addition Tube

F. Mercure-seal Stirrer

G. Thermometer (-50 to 50°C.)

H. Vent Tube

J. Water, Ice or Ice-salt Bath

K. Three-neck, 500-cc. Flask

c. Nitration at Elevated Temperatures

It seemed possible that the large apparent excess of nitric acid was due to incomplete nitration at low temperatures. A twenty percent excess of acid had been allowed but this alone should not have caused oxidation to the extent that was observed. Also, in the article by Thomas, Anzilotti and Hennion (16), which served to suggest the possibility of nitrating carbamates in the presence of boron trifluoride, the nitrations were conducted at elevated temperatures to insure complete reaction. These two factors instigated a study of a series of nitrations at various elevated temperatures.

It was also discovered from a more critical survey of Thomas, Anzilotti and Hennion's paper (16) that only one equivalent of boron trifluoride was used, (i.e. no excess was provided to combine with the water present in the nitric acid used). Therefore, in the following work only the equivalent, 18.7 g. (0.25 mole \nearrow 10% excess), of boron trifluoride was provided.

1.) Nitration 35-40°C.

Approximately 19 g. of boron trifluoride was absorbed in 22 g. of fuming nitric acid at a rate that kept the temperature about 40°C. Then 32.7 g. of ethyl-N-isopropyl carbamate was added dropwise while the reaction temperature was controlled at 35-40°C. Each drop of the carbamate caused a perceptible rise in the temperature. When about one-third of the carbamate had

DECLASSIFICATION

1. This document is being declassified in accordance with the provisions of the President John F. Kennedy Library Act, Public Law 93-411, 104 Stat. 1398, and Executive Order 11652, 30 FR 12893, 1965-3.

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been added a vigorous oxidation started which was indicated by the appearance of heavy nitrogen dioxide fumes. Upon dilution of the residue with water only a few drops of oil settled to the bottom of the aqueous solution.

2.) Nitration at 50-60°C.

The preceding experiment was repeated except that the carbamate was added at 50-60°C. Again each drop of carbamate caused the evolution of nitrogen dioxide. About half of the carbamate had been allowed to react before the mixture foamed out of the flask. When the residue was poured into water no oil settled to the bottom, which indicated that the oxidation had destroyed both the reactants and the products.

been added a vigorous oxidation started which was indicated by the appearance of heavy nitrogen dioxide fumes. Upon addition of the residue with water only a few drops of oil settled to the bottom of the aqueous solution.

2.) Nitration at 50-60°C.

The preceding experiment was repeated except that the carbonate was added at 50-60°C. Again each drop of carbonate ceased the evolution of nitrogen dioxide. About half of the carbonate had been allowed to react before the mixture foamed out of the flask. When the residue was poured into water no oil settled to the bottom, which indicated that the oxidation had destroyed both the reactants and the products.

d. Nitration by the Simultaneous
Addition of Boron Trifluoride
and the Carbamate to the Acid

The final experiment at elevated temperatures consisted of adding the boron trifluoride and the carbamate simultaneously at 40-50°C. The entire reaction was accompanied by the slow evolution of nitrogen dioxide. Only about 8 g. of the carbamate had been added before the reaction mixture began to boil and give off heavy clouds of yellow gas, nitrogen dioxide. The flask was then cooled with a water bath to prevent further oxidation and the reaction mixture was immediately poured into 500 cc. of water. The water became very turbid and slightly yellow. On standing a few hours, a light yellow oil rose to the surface indicating that the starting material, ethyl-N-isopropyl carbamate had been recovered, and that no nitration had taken place.

severe oxidation prevented a quantitative recovery of the product.

5. Nitration by the simultaneous
addition of boron trifluoride
and the carbonate to the acid

The final experiment at elevated temperatures consisted of adding the boron trifluoride and the carbonate simultaneously at 40-50°C. The entire reaction was accompanied by the slow evolution of nitrogen dioxide. Only about 5 g. of the carbonate had been added before the reaction mixture began to boil and give off heavy clouds of yellow gas, nitrogen dioxide. The flask was then cooled with a water bath to prevent further oxidation and the reaction mixture was immediately poured into 500 cc. of water. The water became very turbid and slightly yellow. On standing a few hours, a light yellow oil rose to the surface indicating that the starting material, ethyl-*tert*-isopropyl carbonate had been recovered, and that no nitration had taken place.

e. Nitration by the Addition of
a Mixture of Boron Trifluoride
and Nitric Acid to the Carbamate

The work thus far definitely indicated that the post-reaction oxidation was due to excess nitric acid. It seemed only logical to try adding the acid to the carbamate in order to keep the acidity of the solution at a minimum.

To 32.7 g. of carbamate was added dropwise 22 g. of fuming nitric acid containing 23 g. of boron trifluoride, keeping the temperature between 30°C. and 40°C. The reaction was exothermic and turned yellow as the addition proceeded. After about sixty percent of the acid had been used there was a sharp explosion followed by a vigorous decomposition. The residue yielded only two or three drops of heavier than water material. This further indicated that some degree of nitration always occurred but that severe oxidation prevented a quantitative recovery of the product.

The flask and the reagents weighed two grams less than at the beginning. Each time the water-bath, used to cool the reaction mixture, was removed with the temperature and the nitrogen dioxide evolution increased. The mixture, when poured into 250 cc. of water, settled to the bottom of the aqueous solution, indicating that some nitro compound had been formed. But, several washings completely dissolved the oil. (The carbamate is somewhat soluble in water while the nitrated form is definitely insoluble.) This was evidently similar to that in the previous experiment where the observed acid increased the density sufficiently

a. Nitration by the addition of
a mixture of Boron Trifluoride
and Nitric Acid to the Carbazate

The work thus far definitely indicated that the nitro-
nitric oxidation was due to excess nitric acid. It seemed only
logical to try adding the acid to the carbazate in order to
keep the acidity of the solution at a minimum.

To 32.7 g. of carbazate was added dropwise 22 g. of fuming
nitric acid containing 23 g. of boron trifluoride. Keeping the
temperature between 30°C. and 40°C. The reaction was exother-
mic and turned yellow as the addition proceeded. After about
sixty percent of the acid had been used there was a sharp ex-
plosion followed by a vigorous decomposition. The residue
yielded only two or three drops of heavier than water material.
This further indicated that some degree of nitration always
occurred but that severe oxidation prevented a quantitative re-
covery of the product.

f. Nitration by Absorbing Boron
Trifluoride in a Mixture of
Nitric Acid and the Carbamate

There remained one more uninvestigated method of combining the reactants, that of adding the boron trifluoride to a mixture of fuming nitric acid and ethyl-N-isopropyl carbamate. This was the sequence used by Thomas, Anzilotti and Hennion (16) in the nitration of nitrobenzene and therefore was tested in the following experiment.

A mixture of 14.7 g. (0.17 mole / 20% excess) of acid and 21.8 g. (0.17 mole) of carbamate was prepared at 55-70°C. as described in the first experiments on nitration at elevated temperatures. In this mixture was absorbed a slow stream of boron trifluoride for one-half hour while the temperature was kept between 40°C. and 50°C. During the whole reaction there was a constant evolution of nitrogen dioxide and even after the addition of boron trifluoride the flask and the reagents weighed two grams less than at the beginning. Each time the water-bath, used to cool the reaction mixture, was removed both the temperature and the nitrogen dioxide evolution increased. The mixture, when poured into 250 cc. of water, settled to the bottom of the aqueous solution, indicating that some nitro compound had been formed. But, several washings completely dissolved the oil. (The carbamate is somewhat soluble in water while the nitrated form is definitely insoluble.) This case was evidently similar to that in the previous experiment where the absorbed acid increased the density sufficiently

2. Nitration by Absorbing Boron Trifluoride in a Mixture of Nitric Acid and the Carbamate

There remained one more uninvestigated method of combining the reagents, that of adding the boron trifluoride to a mixture of fuming nitric acid and ethyl-*n*-butoxy carbamate. This was the sequence used by Thomas, Amis, and Henson (15) in the nitration of nitrobenzene and therefore was tested in the following experiment.

A mixture of 14.5 g. (0.15 mole) of acid and 21.2 g. (0.15 mole) of carbamate was prepared at 55-60°C. as described in the first experiments on nitration at elevated temperatures. In this mixture was absorbed a slow stream of boron trifluoride for one-half hour while the temperature was kept between 40°C. and 50°C. During the whole reaction there was a constant evolution of nitrogen dioxide and even after the addition of boron trifluoride the flask and the reagents weighed two grams less than at the beginning. Each time the water-bath, used to cool the reaction mixture, was removed both the temperature and the nitrogen dioxide evolution increased. The mixture, when poured into 250 cc. of water, settled to the bottom of the aqueous solution, indicating that some nitro compound had been formed. But, several washings completely dissolved the oil. (The carbamate is somewhat soluble in water while the nitrated form is definitely insoluble.) This case was evidently similar to that in the previous experiment where the absorbed acid increased the density sufficiently

to make the oil heavier than water; therefore, the initial conclusion that the nitro carbamate had been formed was incorrect. Again, all indications were that no nitro carbamate was prepared.

In a reaction similar to the preceding one the water-bath, used to cool the reaction mixture, was removed as soon as the addition of the gas was completed in order to determine the maximum temperature that would be reached if the oxidation were allowed to proceed freely. The solution began to boil immediately and the temperature rose to 145°C . in about two minutes with an increasing evolution of nitrogen dioxide during the rise. There was a loss of about 25 g. of reaction material as gases during the oxidation. The most amazing observation was that the oxidation, as indicated by the evolution of nitrogen dioxide, ceased suddenly, while still at its maximum, as if it had just been turned off. No doubt, this cessation was due to a lack of any more organic material that could undergo further oxidation. When the residue was poured into water, it settled to the bottom but it dissolved when it was allowed to stand overnight. This indicated that oxidation had completely destroyed any ethyl-N-nitro-N-isopropyl carbamate that might possibly have been formed.

g. Determination of the Temperature at Which Oxidation Occurs

The temperature at which oxidation first started to occur was determined by allowing a reaction mixture to warm slowly after the addition of the carbamate had been completed. To a solution of 20 g. of boron trifluoride in 22 g. of fuming nitric acid prepared at 0-10°C. was added 32.7 g. of ethyl-N-isopropyl carbamate while the temperature of the mixture was maintained between -10°C. and 0°C. The reaction mixture was then permitted to stand in the ice-salt bath with continuous stirring. As the ice melted, the temperature of the mixture rose slowly and the solution became yellow. After two hours the temperature reached 20°C. and began to climb rapidly until there was a vigorous oxidation. The slight residue, when poured into water, settled to the bottom indicating that a small amount of nitro carbamate had been formed. It was concluded that so long as the reaction mixture was kept below 20°C. oxidation would not start. It proved best to work below 10°C. when excess nitric acid was present because temperature fluctuations due to "reaction lag" suddenly warmed the mixture several degrees.

D. Nitration with Absolute Nitric Acid

As was true in the case of fuming nitric acid, a large variety of data has been reported regarding nitrations with 100% nitric acid. These data were of no value for comparison purposes with the results obtained in this thesis because the nitrations had involved the use of a several-fold excess of acid. The object of the present work was the study of the extent of nitration produced when only an equivalent (plus a slight excess) of acid was used. It was therefore necessary to conduct an experiment whose values could be used as a basis in comparing yields.

Similarly, since the major interest of this research was the effect of boron trifluoride on increasing the extent of nitration, it was of equal importance to observe the characteristics and the yield of a reaction of boron trifluoride and absolute nitric acid with the carbamate.

From the data obtained in these two experiments it was possible to determine the actual advantages obtained with the use of boron trifluoride and contrast the relative nitrating power of fuming nitric acid (87%) and absolute nitric acid (100%).

The absolute nitric acid was prepared by distilling it at reduced pressure from a mixture of 75 cc. of fuming nitric acid (87%) and 150 cc. of concentrated sulfuric acid (98%). The distillation was carried out in an entirely glass apparatus (all joints were ground glass).

To 13.5 g. ($1/6$ mole \neq 20% excess) of absolute nitric acid was added dropwise 20.8 g. ($1/6$ mole) of ethyl-N-isopropyl carbamate at $-2-0^{\circ}\text{C}$. The reaction was somewhat exothermic but there were no signs of oxidation. The addition took about forty-five minutes. After fifteen minutes of additional stirring, the reaction mixture was poured into 500 cc. of water at 7°C . with continuous mechanical stirring. The diluent showed no change in temperature as a result of the addition. The oil that settled to the bottom of the aqueous solution was washed once with water, separated, and dried by filtration through dry filter paper. The recovered oil weighed 2.5 g. and had a refractive index at 20°C . of 1.4289. The refractive index of the carbamate and the nitro carbamate at this temperature are 1.4219 (9) and 1.4388 (10) respectively. Assuming that the refractive index of a mixture is approximately a linear function of the percentage of its components, the fraction of nitro carbamate in the oil was determined to be 41.5%. The actual yield of nitro carbamate was therefore only 8.8%.

1.4360. As in the previous experiment, on the basis of its refractive index, the purity of the oil was calculated to be 77.5%. When this correction factor was applied to the amount of oil recovered, the true yield of ethyl-N-nitro-N-isopropyl carbamate was 26.5%.

E. Nitration with Absolute Nitric Acid and Boron Trifluoride

About 15 g. of boron trifluoride was added to 13.5 g. (1/6 mole / 20% excess) of absolute nitric acid at 0-15°C. The absorption was quite exothermic and nitric acid fumes were continuously evolved. The dropwise addition of 21.8 g. (1/6 mole) of ethyl-N-isopropyl carbamate at -5-0°C. took three-quarters of an hour. The stirring was continued an additional thirty minutes while the temperature of the reaction mixture was maintained at -5°C. During the entire reaction there were no signs of oxidation. Upon completion of the stirring, the reaction mixture was poured into 500 cc. of ice and water. There was a constant evolution of white gas (undoubtedly both boron trifluoride and nitric acid) throughout the dilution, but there was no rise in temperature of the solvent. The oil, that settled to the bottom of the aqueous solution, was separated and washed twice with fresh water. Careful separation and repeated filtration through dry filter paper yielded 10 g. of dry light yellow oil whose refractive index at 20°C. was found to be 1.4350. As in the previous experiment, on the basis of its refractive index, the purity of the oil was calculated to be 77.5%. When this correction factor was applied to the amount of oil recovered, the true yield of ethyl-N-nitro-N-isopropyl carbamate was 26.5%.

F. Discussion of Oxidation

It was originally believed that the oxidation, which occurred in almost all the preceding experiments, was merely due to a "reaction lag". As a result of this "lag", large local concentrations of unreacted acid would be present in the reaction mixture. Such an increase in the concentration beyond a critical value would cause the oxidation of the organic materials present.

A more thorough study of the situation was instigated by the seemingly unavoidable oxidation encountered in many of the reactions. The new conclusions reached were not radically different from those outlined in the previous paragraph; however, a more rigorous application of the theory of oxidation to the present problem resulted in several modifications.

It is a well known fact that the nitrate ion is the agent effecting oxidation in a nitric acid solution; hence, the investigation of the possibility of its presence to any extent in the reaction was the initial problem. Since the fuming nitric acid used contained approximately thirteen percent water, a large degree of ionization was possible. Therefore, it is obvious that the addition of water, as was true in the first few reactions with boron trifluoride and fuming nitric acid when the recovery of the boron trifluoride was attempted, was not necessary for the formation of the nitrate ion. In fact, the nitrate ions were present throughout all the reactions, but it was not until a local concentration developed that actual

observation of the decomposition due to oxidation was possible.

If the conclusions reached in the previous paragraph were true, oxidation should not occur when only traces of water are present. The complete lack of oxidation in the experiments with absolute nitric acid substantiated the latter explanation for the decomposition due to oxidation of the organic components of the reactions.

It was desirable, therefore, to conduct a similar series of nitrations on a carbonate that was more stable towards nitric acid. Ethyl- β -methyl carbonate was used because none of the hydrogens on the alpha carbon would be unusually active.

Table II

Reagent	Mole Equivalent	Moles Used	Grams Used
Ethyl- β -methyl carbonate	0.17	0.17	17.3
Nitric Acid (67%) (10% excess)	0.17 <u>0.08</u>	0.17	16.3
Water present in acid (12%)	0.11		1.08
Boron trifluoride (10% excess) (as dehydrated)	0.17 0.08 <u>0.11</u>	0.33	21.3

Approximately 21 g. of boron trifluoride was absorbed in 16.3 g. of fuming nitric acid at 10°C. To this was added dropwise 17.3 g. of ethyl- β -methyl carbonate while the temperature

III. NITRATION OF ETHYL-N-METHYL CARBAMATE

A. Nitration with fuming Nitric Acid and Boron Trifluoride

In the preceding experiments the nitrations with fuming nitric acid were accompanied by some degree of oxidation. This occurrence substantiated Thomas's (15) theories regarding the easy oxidation of the isopropyl structure due to the active hydrogen on the central carbon. It was desirable, therefore, to conduct a similar series of nitrations on a carbamate that was more stable towards nitric acid. Ethyl-N-methyl carbamate was used because none of the hydrogens on the alpha carbon would be unusually active.

Table II

Reagent	Mole Equivalent	Moles Used	Grams Used
Ethyl-N-methyl carbamate	0.17	0.17	17.3
Nitric Acid (87%) (10% excess)	0.17 <u>0.02</u>	0.19	15.2
Water present in acid (13%)	0.11		1.98
Boron trifluoride (10% excess) (to dehydrate acid)	0.17 0.02 <u>0.11</u>	0.30	20.3

Approximately 21 g. of boron trifluoride was absorbed in 15.2 g. of fuming nitric acid at 10°C. To this was added dropwise 17.3 g. of ethyl-N-methyl carbamate while the temperature

was kept below -5°C . After the addition was completed the ice-salt cooling bath was removed and the reaction mixture was allowed to warm slowly. As it warmed, heavy white fumes (probably boron trifluoride) were evolved. When the temperature of the reaction mixture reached 30°C ., it began to boil and give off nitrogen dioxide. The solution was immediately poured into 200 cc. of water in order to prevent further oxidation. An oil slowly settled to the bottom of the aqueous solution. This oil was separated and dried by filtering it through several layers of dry filter paper.

For the dry oil, $n_D^{23} = 1.4451$. The refractive index of ethyl-Nitro-N-methyl carbamate is recorded in the literature as $n_D^{23} = 1.44826$ (2). The oil was then distilled under reduced pressure without difficulty although the compound is reported to have exploded when distillation was attempted. (7) Boiling point, $73-74^{\circ}\text{C}$. at 2.5 mm.; $n_D^{23} = 1.4469$ and $n_D^{20} = 1.4480$; Yield, 12.0 (50.7%). This rise in the refractive index as a result of distillation was not unusual. It has been noted before with other nitro carbamates that the higher the purity, the higher the index. In the paper by Bruhl (2) originally reporting this compound the index was undoubtedly taken on the crude material because he does not record any successful attempts at distillation. There seemed reason to doubt that the reported value of $n_D^{23} = 1.44826$ because in this and in subsequent work after careful and reported distillation an index of $n_D^{23} = 1.4470$ was found.

1. The Effect of the Temperature on Nitration

The foregoing experiment was repeated with some modifications at the end in order to determine the temperature at which oxidation would take place. There also remained a doubt as to whether the boiling that occurred at 30°C. was due to continued nitration at a higher temperature or, as presumed, merely the first sign of oxidation.

The initial preparation of the nitro carbamate was similar to that in the preceding experiment except that the reaction mixture was kept below -30°C. while the carbamate was added. The reaction mixture was then cooled to -10°C., divided into three portions and treated as follows: 16 cc. was poured into ice water, 8 cc. was allowed to warm to 30°C. and then poured into water, and the remaining 8 cc. was permitted to warm until it completely oxidized.

The first portion was allowed to stand overnight in its aqueous solution. A small amount of solid appeared in the oil but it was found to be water soluble after the solution was shaken vigorously several times. It was undoubtedly some inorganic salt. The solution was extracted with 25 cc. of ether which was then dried with sodium carbonate, filtered and evaporated. The ethyl-N-nitro-N-methyl carbamate, which was recovered, was a light yellow oil; yield, 6.6 g.; $n_D^{20} = 1.4475$. This refractive index indicated that the product was only slightly impure.

The second fraction evolved white fumes (excess boron

trifluoride) when it was warmed. As the temperature increased, the fumes became more dense. The action was not exothermic below 22°C. At 25°C. ebullition began, and the temperature rose sharply to 29°C. At this point the boiling and the gaseous evolution became very vigorous. The reaction mixture was quickly poured into 100 cc. of water at 14°C. As a result, the water's temperature rose to 32°C., indicating that the oxidation was not stopped immediately by the dilution. The aqueous solution was extracted with 25 cc. of ether which was dried, filtered and evaporated. The residue was a dirty yellow oil; yield, 3.4 g.; $n_D^{20} = 1.4461$. This oil was therefore slightly less pure than the oil recovered from the preceding fraction. This was attributed to the small amount of decomposition caused by oxidation at 30°C.

The last 8 cc. acted the same way as the second portion as it warmed to 30°C. The temperature then began to rise at the rate of a degree per second. The solution turned a bright yellow at 35°C. A few cubic centimeters were removed at 45°C. At 65-70°C. heavy nitrogen dioxide fumes were evolved and part of the liquid foamed out of the beaker. The temperature finally reached a maximum of 100°C. and then dropped sharply to 40°C. Only about 1 cc. of tarry residue was left in the beaker after the oxidation was completed.

The portion extracted at 45°C. was instantly poured into about 10 cc. of water. An oil rose to the surface but it was insoluble in water even after further dilution and prolonged

shaking. Ethyl-N-methyl carbamate is water soluble and the nitro carbamate is insoluble but also heavier than water; so, this oil was neither of these. Recent investigations have shown that the oxidation of ethyl-N-nitro-N-isopropyl carbamate with alkaline permanganate yielded N-nitro-isopropylamine, (4), but no detailed study has been made regarding the oxidation product of fuming nitric acid. It may be possible that this unidentified oil was N-nitro-methylamine.

The yield from the first two portions checked within 0.1 g. which was within the experimental error of the balances used. (First portion -- 16 cc. yielded 6.6 g., or for 8 cc. a yield of 3.3 g.; second portion -- 8 cc. yielded 3.4 g.) Figured on the basis of the second portion, the over-all yield for the reaction was 13.6 g. (59.3%). Therefore, it was concluded that so long as the reaction was kept below 30°C. (this does not refer to the temperature during the reaction but to the temperature after the reaction was completed) there would be no oxidation. But obviously, from a comparison of the refractive indexes of the first and second portions, the higher the temperature was allowed to go, the lower the purity of the crude product. This second experiment also proved that the boiling at 30°C. was not continued nitration but merely the beginning of oxidation.

B. Solubility of Ethyl-N-nitro-N-methyl Carbamate in Water

Since the ethyl-N-methyl carbamate was highly soluble in water, 94.7g/100cc (7), it seemed possible that the nitro carbamate would not be entirely insoluble as was true in the case of ethyl-N-nitro-N-isopropyl carbamate. No data regarding the solubility of ethyl-N-nitro-N-methyl carbamate was found in the literature; so, a rough determination of its solubility was made in the following manner.

One cc. of ethyl-N-nitro-N-methyl carbamate was pipetted into a 250-cc. flask. Water, at 15°C., was added a few cubic centimeters at a time with continuous agitation. The nitro carbamate was completely dissolved by 75 cc. of water. For the nitro carbamate $d_4^{23} = 1.2288$ (2), therefore, the approximate solubility was 1.23g/75cc, or 1.64g/100cc at 15°C.

In order to determine the relative solubility of the nitro carbamate in water and ether, the solution was extracted with 25 cc. of ether. The ether was dried over anhydrous sodium carbonate for thirty minutes, filtered into a weighing bottle and evaporated. The oil recovered weighed 0.58 g. Hence, less than half of the completely soluble material (the nitro carbamate) could be regained. This indicated that a single ether extract removed only about 50% of the dissolved nitro carbamate.

In the last experiment, the first portion of the yield was poured into 100 cc. of water. Therefore, about 1.64 g. was dissolved in the water, of which only 0.7 g. was recovered

E. Solubility of Ethyl-N-nitro-N-methyl carbamate
in water

Since the ethyl-N-methyl carbamate was highly soluble in water, 94.75/100 (7), it seemed possible that the nitro carbamate would not be entirely insoluble as was true in the case of ethyl-N-nitro-N-isopropyl carbamate. No data regarding the solubility of ethyl-N-nitro-N-methyl carbamate was found in the literature; so, a rough determination of its solubility was made in the following manner.

One cc. of ethyl-N-nitro-N-methyl carbamate was pipetted into a 150-cc. flask. Water, at 15°C., was added a few cubic centimeters at a time with continuous agitation. The nitro carbamate was completely dissolved by 75 cc. of water. The nitro carbamate $d_4^{25} = 1.2888$ (8), therefore, the approximate solubility was 1.2888/100, or 1.2888/100 at 15°C.

In order to determine the relative solubility of the nitro carbamate in water and ether, the solution was extracted with 25 cc. of ether. The ether was added over anhydrous sodium carbonate for thirty minutes, filtered into a weighing bottle and evaporated. The oil recovered weighed 0.55 g. Hence, less than half of the completely soluble material (the nitro carbamate) could be recovered. This indicated that a single ether extract removed only about 50% of the dissolved nitro carbamate.

In the next experiment, the first portion of the yield was poured into 100 cc. of water. Therefore, about 1.64 g. was dissolved in the water, of which only 0.5 g. was recovered

leaving a net loss of 0.9 g. If this loss were added to the recovered material, 6.6 g., there would have been 7.5 g. Since this was for only half of the reaction, 15.0 g. was the total ethyl-N-nitro-N-methyl carbamate formed. This would mean that the conversion to the nitro carbamate was at least 65%. If the preceding correction factor were applied to the nitro carbamate obtained from the second portion in the previous experiment, a conversion of over 70% can be assumed to have occurred.

leaving a net loss of 0.9 g. If this loss were added to the recovered material, 3.3 g., there would have been 3.3 g. since this was for only half of the reaction, 16.0 g. was the total ethyl-2-nitro-3-methyl carbamate formed. This would mean that the conversion to the nitro carbamate was at least 65%. If the preceding correction factor were applied to the nitro carbamate obtained from the second portion in the previous experiment, a conversion of over 70% can be assumed to have occurred.

Table III

During the course of the preceding work the following physical constants were either determined or found in the literature.

Carbamate	Boiling Point 760 mm.	Reduced Pressure	Refractive Index n_D^{20} Indicated
Ethyl-N-isopropyl	176° (9)	88-92° @ 25mm * 85° @ 15mm (11)	1.4231 (10) # 1.4219 (9)
Ethyl-N-methyl	170° (13)	87° @ 35mm * 80° @ 14.5mm (12)	1.4189 * # 1.4200 @ 18.9° (12)
Ethyl-N-nitro- N-isopropyl	decomposes (10)	62-64° @ 6mm (3)	1.4388 (10) #
Ethyl-N-nitro- N-methyl	explodes over 100° (7)	73-74° @ 2.5mm *	1.4480 * # 1.44826 @ 23° (2) 1.4469 @ 23° * #

* Values determined during the course of this research

Values obtained by using an Abbe refractometer with an initial heterocromatic light source. The same instrument was used for determining the refractive index of the nitration products in order to find the purity of the yield.

Table IV

No.	Ethyl Carbamate	Method of Nitration*	Temperature °C.
1.	Isopropyl	Nitric Acid	55-70
2.	Isopropyl	Nitric Acid and concentrated Sulfuric Acid	25-40
3.	Isopropyl	Nitric Acid and Boron Trifluoride; then Water added	below 10
4.	Isopropyl	Nitric Acid and Boron Trifluoride Reaction Mixture added to a Large Volume of Water	below 0
5.	Isopropyl	Nitric Acid and Boron Trifluoride; then Calcium Hydroxide added	below 10
6.	Isopropyl	Nitric Acid and Boron Trifluoride	35-40
7.	Isopropyl	Nitric Acid and Boron Trifluoride	50-60
8.	Isopropyl	Simultaneous addition of Carbamate and Boron Trifluoride to Nitric Acid	40-50
9.	Isopropyl	Mixture of Nitric Acid and Boron Trifluoride added to Carbamate	30-40
10.	Isopropyl	Boron Trifluoride added to a mixture of Nitric Acid and Carbamate	-----
11.	Isopropyl	100% Nitric Acid	-5-0

* Unless otherwise indicated fuming nitric acid was used and the carbamate was added to the acid

Table IV (continued)

No.	Ethyl Carbamate	Method of Nitration	Temperature °C.		
12.	Isopropyl	100% Nitric Acid and Boron Trifluoride	-2-0		
13.	Methyl	Nitric Acid and Boron Trifluoride	below -5		
14.	Methyl	Nitric Acid and Boron Trifluoride	-5-40		
No.	Yield in Grams	Purity %	Theoretical Yield	Yield %	Comments
1.	No Nitration	-	-	-	Even after 24 hours contact
2.	-	-	-	-	Oxidation
3.	-	-	-	-	Oxidation when water added
4.	Fair	-	-	-	Yield not weighed
5.	-	-	-	-	Oxidation when calcium hydroxide added
6.	-	-	-	-	Oxidation
7.	-	-	-	-	Oxidation
8.	No Nitration	-	-	-	Oxidation

IV. NITRATION OF CARBAMATES IN THE PRESENCE OF INORGANIC OXIDIZING AGENTS

The investigations thus far had been decidedly unproductive.

Except for those with 100% nitric acid. In the nitration of carbamates with nitric acid, only those of which the nitration was to be studied were used. In the nitration of carbamates with nitric acid, only those of which the nitration was to be studied were used. In the nitration of carbamates with nitric acid, only those of which the nitration was to be studied were used.

Table IV (concluded)

No.	Yield in Grams	Purity %	Theoretical Yield	Yield %	Comments
9.	Traces	-	-	-	Oxidation
10.	No Nitration	-	-	-	Oxidation
11.	2.5	41.5	28.4	8.8	
12.	10.0	77.5	29.3	26.5	
13.	12.0	100.0	24.1	50.7	
14.	13.6	100.0	24.1	59.3	

IV. NITRATION OF CARBAMATES IN THE PRESENCE OF INORGANIC DEHYDRATING AGENTS

The investigations thus far had been decidedly unsuccessful, except for those with 100% nitric acid. In the nitrations with fuming nitric acid, only those of ethyl-N-methyl carbamate were satisfactory to the extent that it was possible to control the reaction and recover the product. In the other nitrations, the reaction either did not go or oxidation destroyed the yield.

Deliquescent inorganic salts offered a heretofore uninvestigated method of dehydrating the reaction mixtures. In the following reactions enough salt, either anhydrous sodium sulfate or sodium bisulfate, was provided to combine with both the water in the fuming nitric acid (when present) and the water produced in the nitration.

The first group of experiments depended on the dehydrating effect of sodium bisulfate which was a by-product of the preparation of nitric acid from sodium nitrate and sulfuric acid. One mole of acid sulfate would have taken up one mole of water in the formation of its hydrate but a 100% excess was allowed in order to insure complete dehydration. Therefore, in nitrating one mole of the carbamate, two moles of sodium nitrate and two of sulfuric acid were used. Three moles more of acid was employed as a reaction solvent, which made a total of five moles.

In the second series of nitrations an equivalent plus a

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20% excess of fuming nitric acid was utilized. The dehydration was accomplished with anhydrous sodium sulfate, which can combine with ten moles of water.

A. Nitration of Ethyl-N-isopropyl Carbamate

1. Nitration with Sodium Nitrate and Sulfuric Acid

a. At 0°C.

A mixture of 42.5 g. (0.5 mole) of sodium nitrate and 122.5 g. (1.25 moles) of concentrated sulfuric acid was prepared at room temperature. To this was added 32.7 g. (0.25 mole) of ethyl-N-isopropyl carbamate with continuous stirring while the reaction mixture was kept at 0°C. The reaction did not seem to be exothermic during any of the addition. The stirring was continued for an hour after which the solid was filtered off and the filtrate diluted with 1 liter of water. An oil rose to the surface and smelled like the starting material. It was presumed to be the unreacted carbamate.

An identical experiment was conducted on 1/6 mole of the carbamate but slightly different observations were made. Twenty-eight and four-tenths grams of sodium nitrate and 81.6 g. of concentrated sulfuric acid were mixed at room temperature in a 3-neck 500-cc flask and cooled immediately to 0°C. Then 21.8 g. of carbamate was added dropwise while the reaction mixture was kept at this temperature. The reaction was slightly exothermic and the temperature fluctuated depending on the rate of the addition. Upon completion of the addition the reaction mixture was still a gray-white sirup. After stirring for another half-hour, it was poured into 300 cc. of water containing 100 g. of ice. This solvation was quite exothermic due to the presence of sulfuric acid. The water turned yellow

and an oil floated to the surface while a solid settled to the bottom. The oil was separated and added to 400 cc. of fresh water, but the oil still rose to the surface. It was again separated and dried by filtering it through several dry filter papers. About 6 g. of clear light yellow oil was recovered, $n_D^{20} = 1.4243$. The refractive indexes of the carbamate and nitro carbamate at 20°C. are 1.4219 (9) and 1.4388* respectively. It was assumed that the refractive index of a mixture was approximately a linear function of the percentage of its components. On this basis the nitrated portion of the yield was calculated as 24/169 or almost 15%. This gave an over-all yield of only 3%.

b. At 12-15°C.

If some degree of nitration were possible at 0°C., it seemed logical to expect that more would occur at a higher temperature. However, this did not prove to be the case, instead the nitrated fraction was less than half as great. This was undoubtedly due to some oxidation. A reaction mixture for 1/6 mole of carbamate was prepared as in the preceding experiment and to this was added dropwise 21.8 g. of ethyl-N-isopropyl carbamate while the temperature was kept at 12-15°C. The reaction was only slightly exothermic and the addition was completed in twenty minutes. There were no signs of oxidation during the reaction or in the fifteen minutes of stirring that followed. The reaction mixture was then poured into 300 cc. of

*Determined during the experimental work for this thesis

ice and water. The oil that separated remained suspended in the center of the aqueous solution. This oil was extracted with 40 cc. of ether. The ethereal extract was light yellow but when it was poured over anhydrous potassium carbonate to dry it turned dark orange. Although no nitrogen dioxide was evolved it was believed that this indicated further oxidation. After fifteen minutes the ethereal solution was filtered and the ether evaporated. The cloudy orange oil that was left was further dried by filtering it through dry filter paper. As a result a clear light yellow oil was obtained. Yield, about 5 g. $n_D^{20} = 1.4230$. The oil was again tested and found to be lighter than water. On the basis of the refractive index the purity of the oil was calculated to be 7% and the true yield of nitro carbamate was therefore 1.2%. As previously stated, the purity and yield are both lower at the elevated temperature.

c. At 40°C.

A reaction mixture of 28.4 g. of sodium nitrate and 81.6 g. of concentrated sulfuric acid for the nitration of one sixth of a mole of ethyl-N-isopropyl carbamate was again prepared at room temperature. When the mixture cooled to 40°C. the dropwise addition of 21.8 g. of ethyl-N-isopropyl carbamate was started. After three drops had been added the temperature began to rise. At the end of ten drops it was 70°C. and heavy clouds of nitrogen dioxide were being evolved. The addition was stopped and the reaction flask was placed in a water bath at 10°C. but it was five minutes before the temperature of the

reaction mixture began to drop. The gas slowly cleared away revealing a reaction mixture that was almost entirely solid instead of the heavy sirup that was present in the beginning. This reaction therefore was discontinued because the addition of the carbamate was accompanied by continuous oxidation.

After evacuating the flask and then allowing cool air, which had been dried by passing it over a mixture of anhydrous calcium chloride and sodium carbonate, to flow back into the flask, the sodium sulfate was immediately added to the reaction.

g. Nitric Acid and Carbamate con-
tained; then Sodium Sulfate added

To 21.8 g. (1/6 mole) of ethyl-2-isopropyl carbamate was added dropwise 14.7 g. (1/6 mole + 40% excess) of fuming nitric acid with stirring, while the temperature ranged between 25°C. and 40°C. Six grams of freshly calcined sodium sulfate was added to the acid-carbamate mixture which had been stirred for forty-five minutes. The reaction was allowed to stand overnight and then was decanted into 150 cc. of water. The oil that rose to the surface was separated and added to 50 cc. of fresh water. The oil again came to the surface and was there-fore extracted with 50 cc. of ether. The etheral solution was dried over anhydrous potassium carbonate. The ether was distilled at atmospheric pressure and the oil at reduced pressure. B.P., 53-54°C. at 5 mm.; $n_D^{20} = 1.4541$. On the basis of this refractive index the nitro carbamate portion of the yield

reaction mixture began to drop. The gas slowly cleared away revealing a reaction mixture that was almost entirely solid instead of the heavy sludge that was present in the beginning. This reaction therefore was discontinued because the addition of the carbonate was accompanied by continuous oxidation.

2. Nitration with fuming Nitric Acid and anhydrous Sodium Sulfate

The sodium sulfate used in this and following experiments was freshly calcined before each reaction. It was heated at 260°C. for thirty minutes and then cooled in a vacuum over concentrated sulfuric acid. The cooling was hastened by alternately evacuating the desiccator and then allowing cool air, which had been dried by passing it over a mixture of anhydrous calcium chloride and sodium carbonate, to flow back into the desiccator. The sodium sulfate when cool was immediately used in the reaction.

a. Nitric Acid and Carbamate combined; then Sodium Sulfate added

To 21.8 g. (1/6 mole) of ethyl-N-isopropyl carbamate was added dropwise 14.7 g. (1/6 mole \neq 40% excess) of fuming nitric acid, with stirring, while the temperature ranged between 25°C. and 40°C. Six grams of freshly calcined sodium sulfate was added to the acid-carbamate mixture which had been stirred for forty-five minutes. The reaction was allowed to stand overnight and then was decanted into 150 cc. of water. The oil that rose to the surface was separated and added to 25 cc. of fresh water. The oil again came to the surface and was therefore extracted with 50 cc. of ether. The ethereal solution was dried over anhydrous potassium carbonate. The ether was distilled at atmospheric pressure and the oil at reduced pressure. B.P., 62-64°C. at 6 mm.; $n_D^{20} = 1.4241$. On the basis of this refractive index the nitro carbamate portion of the yield

S. Nitration with Fuming Nitric Acid
and anhydrous Sodium Sulfate

The sodium sulfide used in this and following experiments was freshly calcined before each reaction. It was heated at 280°C. for thirty minutes and then cooled in a vacuum over concentrated sulfuric acid. The cooling was hastened by allowing the flask containing the flask and then allowing cool air, which had been dried by passing it over a mixture of anhydrous calcium chloride and sodium carbonate, to flow back into the flask. The sodium sulfide when used was immediately used in the reaction.

S. Nitric Acid and Carbonate com-
bined; then Sodium Sulfate added

To 21.8 g. (1/6 mole) of ethyl-2-isopropyl carbonate was added dropwise 14.7 g. (1/6 mole - 40% excess) of fuming nitric acid, with stirring, while the temperature ranged between 25°C. and 40°C. Six grams of freshly calcined sodium sulfide was added to the acid-carbonate mixture which had been stirred for forty-five minutes. The reaction was allowed to stand overnight and then was decanted into 150 cc. of water. The oil that rose to the surface was separated and added to 25 cc. of fresh water. The oil again came to the surface and was there-fore extracted with 50 cc. of ether. The etheral solution was dried over anhydrous potassium carbonate. The ether was distilled at atmospheric pressure and the oil at reduced pressure. B.P. 62-64°C. at 5 mm.; n_D^{20} 1.4441. On the basis of this refractive index the oil is carbonate portion of the yield

was calculated to be 22/169 or about 13%.

b. Carbamate added to a Mixture of Nitric Acid and Sodium Sulfate

In a second experiment along the same line the carbamate was added to a mixture of the anhydrous salt and the acid. Six grams of freshly calcined sodium sulfate was mixed with 14.7 g. of fuming nitric acid in a 3-neck 500-cc flask. To this was added, 21.8 g. of ethyl-N-isopropyl carbamate while the temperature was kept between -5°C . and 2°C . When the first few drops were added, the reaction mixture turned dark yellow. After about half of the carbamate had been used, the solution became a much lighter yellow. The addition took over an hour but it was not difficult, during this period of time, to maintain the temperature below 0°C . The stirring was continued an additional thirty minutes after the addition had been completed. The reaction mixture was then poured into 200 cc. of water at 7°C ., but only a slight elevation in temperature was noted. A light yellow oil rose to the surface of the aqueous solution while a solid (inorganic salt) settled to the bottom. The lower water layer was separated by using a separatory funnel, and to the oil layer was added 200 cc. of fresh water with vigorous shaking. The oil, which again rose to the surface, was separated and dried by filtration through dry filter paper. A clear light yellow oil was recovered. Yield, about 11 g.;

$n_{\text{D}}^{20} = 1.4233$. As before, on the basis of this refractive index the fraction of pure nitro carbamate was calculated to be

was calculated to be 82/100 or about 18%.

D. Carbanate added to a mixture of
Nitric acid and Sodium Chloride

In a second experiment along the same line the carbanate

was added to a mixture of the anhydrous salt and the acid. Six

grams of freshly obtained sodium chloride was mixed with 14.7 g.

of fuming nitric acid in a 3-neck 500-cc flask. To this was

added, 31.8 g. of ethyl-2-isopropyl carbanate while the temper-

ature was kept between -5°C. and 20°C. When the first few drops

were added, the reaction mixture turned dark yellow. After

about half of the carbanate had been used, the solution became

a much lighter yellow. The addition took over an hour but it

was not difficult. During this period of time, to maintain the

temperature below 0°C. The stirring was continued an additional

thirty minutes after the addition had been completed. The re-

action mixture was then poured into 500 cc. of water at 70°C.,

but only a slight elevation in temperature was noted. A light

yellow oil rose to the surface of the aqueous solution while a

solid (inorganic salt) settled to the bottom. The lower water

layer was separated by using a separatory funnel, and to the

oil layer was added 500 cc. of fresh water with vigorous shak-

ing. The oil, which again rose to the surface, was separated

and dried by filtration through dry filter paper. A clear

light yellow oil was recovered. Yield, about 11 g.

$n_D^{20} = 1.4235$. As before, on the basis of this refractive index

the fraction of pure nitro carbanate was calculated to be

14/169 or 8.3%.

In the last six experiments it will be noted that the maximum purity of the oil was 15% and the largest yield of nitro carbamate was only 3%. The purity and hence the yield may have been much smaller; for, traces of nitrogen dioxide present in the oil would have affected the refractive index to some extent. Therefore, it was assumed that these results were insignificant when considered in the light of other possible methods of nitrating ethyl-N-isopropyl carbamate.

To a mixture of 20.4 g. (1/6 mole) of sodium nitrate and 21.6 g. (5/6 mole) of concentrated sulfuric acid was added dropwise 21.6 g. (1/6 mole) of ethyl-N-isopropyl carbamate while the temperature of the reaction mixture was kept at 15-17°C. During the entire addition, which was completed in one-half hour, there were no signs of oxidation. After the reaction mixture had stirred an additional fifteen minutes, it was a gray-white slurry. This slurry was poured into 300 cc. of ice and water. The white oil that settled at the bottom of the aqueous solution was extracted twice with 25 cc. portions of ether. The ethereal solution was dried over anhydrous potassium carbonate, filtered, and the ether evaporated. About 10 g. of almost colorless oil was obtained, n_D^{20} 1.4430. Since the refractive indexes of the carbamate and the nitro carbamate were found to be 1.4189* and 1.4450* respectively at 20°C., the purity of the product was calculated as 250/291 or about 86%.

*Values determined during the experimental work for this thesis

14/108 or 8.3%

In the last six experiments it will be noted that the maximum purity of the oil was 15% and the largest yield of nitro carbonate was only 3%. The purity and hence the yield may have been much smaller; for, traces of nitrogen dioxide present in the oil would have affected the relative index to some extent. Therefore, it was assumed that these results were insignificant when considered in the light of other possible methods of nitrating ethyl-N-isopropyl carbonate.

B. Nitration of Ethyl-N-methyl Carbamate

Since the nitration of ethyl-N-methyl carbamate in the presence of boron trifluoride had been so successful, it was highly possible that these inorganic salts that were tried as dehydrating agents might give satisfactory yields with this carbamate. In the following experiments, one with sodium nitrate and sulfuric acid and the other with anhydrous sodium sulfate, this supposition was substantiated.

1. Nitration with Sodium Nitrate and Sulfuric Acid

To a mixture of 28.4 g. (1/3 mole) of sodium nitrate and 81.6 g. (5/6 mole) of concentrated sulfuric acid was added dropwise 21.8 g. (1/6 mole) of ethyl-N-methyl carbamate while the temperature of the reaction mixture was kept at 15-17°C. During the entire addition, which was completed in one-half hour, there were no signs of oxidation. After the reaction mixture had stirred an additional fifteen minutes, it was a gray-white sirup. This sirup was poured into 300 cc. of ice and water. The white oil that settled to the bottom of the aqueous solution was extracted twice with 25 cc. portions of ether. The ethereal solution was dried over anhydrous potassium carbonate, filtered, and the ether evaporated. About 10 g. of almost colorless oil was obtained, $n_D^{20} = 1.4439$. Since the refractive indexes of the carbamate and the nitro carbamate were found to be 1.4189* and 1.4480* respectively at 20°C., the purity of the product was calculated as 250/291 or about 86%.

*Values determined during the experimental work for this thesis

B. Nitration of Ethyl-N-methylcarbamate

Since the nitration of ethyl-N-methylcarbamate in the presence of boron trifluoride had been so successful, it was highly possible that these inorganic salts that were tried as dehydrating agents might give satisfactory yields with this carbamate. In the following experiments, one with sodium nitrate and sulfuric acid and the other with anhydrous sodium sulfate, this supposition was substantiated.

1. Nitration with Sodium Nitrate and Sulfuric Acid

To a mixture of 28.4 g. (1/5 mole) of sodium nitrate and 21.6 g. (5/6 mole) of concentrated sulfuric acid was added dropwise 21.8 g. (1/5 mole) of ethyl-N-methylcarbamate while the temperature of the reaction mixture was kept at 15-17°C. During the entire addition, which was completed in one-half hour, there were no signs of oxidation. After the reaction mixture had stirred an additional fifteen minutes, it was a gray-white slurry. This slurry was poured into 500 cc. of ice and water. The white oil that settled to the bottom of the aqueous solution was extracted twice with 25 cc. portions of ether. The etheral solution was dried over anhydrous potassium carbonate, filtered, and the ether evaporated. About 10 g. of almost colorless oil was obtained, $n_D^{20} = 1.4450$. Since the refractive indexes of the carbamate and the nitro carbamate were found to be 1.4189 and 1.4480 respectively at 20°C., the purity of the product was calculated as 850/871 or about 86%. Values determined during the experimental work for this thesis

If this factor of purity is introduced into the calculations, the true yield of nitro carbamate becomes 35%. This value compares quite favorably with other methods of nitration by early investigators. It should also be mentioned at this point that although 10 g. of oil was obtained, some was spilled in handling and no precautions were used to insure the recovery of the entire yield from the reaction mixture. The main interest of this work was not in the magnitude of the yields but in determining if nitration would occur.

2. Nitration with fuming Nitric Acid and anhydrous Sodium Sulfate

When 6 g. of freshly calcined sodium sulfate was mixed with 14.7 g. ($1/6$ mole \neq 40% excess) of fuming nitric acid, a deep yellow solution was formed, but as 17.2 g. ($1/6$ mole) of ethyl-N-methyl carbamate was added dropwise at 5-10°C., the solution became much lighter. Although the reaction was slightly exothermic there were no signs of oxidation. The reaction mixture was stirred fifteen minutes after the addition was completed and then poured into 300 cc. of water at 15°C. No oil separated but the water became cloudy. When 25 cc. of ether was shaken with the aqueous solution, no ether layer separated. After 25 cc. more of ether was added, a layer of about 35 cc. of ether was recovered. The ethereal solution was separated, dried over anhydrous potassium carbonate, filtered, and the ether evaporated. Filtration through dry filter paper yielded almost 3 g. of clear yellow oil. The refractive index at 20°C.

If this factor of purity is introduced into the calculations, the true yield of nitro carbonate becomes 38%. This value compares quite favorably with other methods of nitration by early investigators. It should also be mentioned at this point that although 10 g. of oil was obtained, some was spilled in handling and no precautions were used to insure the recovery of the entire yield from the reaction mixture. The main interest of this work was not in the magnitude of the yields but in determining if nitration would occur.

2. Nitration with fuming nitric acid and anhydrous sodium sulfate

When 3 g. of freshly calcined sodium sulfate was mixed with 14.7 g. (1 1/5 mole 1/3 excess) of fuming nitric acid, a deep yellow solution was formed, but as 14.2 g. (1 1/5 mole) of ethyl-N-methyl carbonate was added dropwise at 5-10°C., the solution became much lighter. Although the reaction was slightly exothermic there were no signs of oxidation. The reaction mixture was stirred fifteen minutes after the addition was completed and then poured into 300 cc. of water at 15°C. No oil separated but the water became cloudy. When 25 cc. of ether was shaken with the aqueous solution, no other layer separated. After 25 cc. more of ether was added, a layer of about 25 cc. of ether was recovered. The ethereal solution was separated, dried over anhydrous potassium carbonate, filtered, and the ether evaporated. Filtration through dry filter paper yielded almost 3 g. of clear yellow oil. The refractive index at 20°C.

was found to be 1.4299, and the nitro carbamate fraction was determined to be 10/291 or a little over 3%. The grams of oil recovered evaluated in terms of its purity gave as a true yield of nitro carbamate a value of less than 0.5%.

Table V

No.	Ethyl Carbamate	Method of Nitration	Temperature °C.
1.	Isopropyl	Sodium Nitrate and Sulfuric Acid	0
2.	Isopropyl	Sodium Nitrate and Sulfuric Acid	12-15
3.	Isopropyl	Sodium Nitrate and Sulfuric Acid	40
4.	Isopropyl	Nitric Acid and Sodium Sulfate	----
5.	Isopropyl	Nitric Acid and Sodium Sulfate	-5-2
6.	Methyl	Sodium Nitrate and Sulfuric Acid	15-17
7.	Methyl	Nitric Acid and Sodium Sulfate	5-10

No.	Yield Grams	Purity %	Theoretical Yield	Grams of Pure Nitro Carbamate	Yield %
1.	6	15	29.7	0.9	3.0
2.	5	7	29.7	0.35	1.2
3.	0	0	29.7	0.0	0.0
4.	-	15	29.7	----	----
5.	11	8.3	29.7	0.91	3.1
6.	10	86	24.7	8.6	34.8
7.	3	3	24.7	0.09	0.46

C. Discussion of Results

The only adequate nitration was that of ethyl-N-methyl carbamate with fuming nitric acid and anhydrous sodium sulfate. The dehydrating effect of sodium sulfate probably was not the determining factor in the magnitude of the yield. The extent of nitration when only fuming nitric acid is used was not investigated and its effect alone may account for a large portion of the product.

As for the other reactions, the yields were very poor. Undoubtedly more careful control of the nitrations would net yields of the order of ten percent, but even such an amount would still be insignificant. This lack of nitration was attributed directly to the oxidation which occurred to some extent in most of the reactions. The oxidations were especially prevalent in the nitrations of ethyl-N-isopropyl carbamate. This was also found to be the case in the reactions where boron trifluoride was employed. It will be noted (Table V) that in those reactions with sodium nitrate, sulfuric acid and ethyl-N-isopropyl carbamate, increased temperature decreased the extent of the nitration. This was unquestionably due to oxidation which occurs more readily at the elevated temperatures.

In general, the results of this series of nitrations definitely indicate that anhydrous inorganic salts are not satisfactory dehydrating agents.

V. SUMMARY

New methods of nitrating two carbamates, ethyl-N-isopropyl carbamate and ethyl-N-methyl carbamate, were studied. The effect of various dehydrating agents (boron trifluoride, sodium bisulfate, and anhydrous sodium sulfate), the order of the addition of the reactants, and the optimum temperature of reaction were investigated. The majority of this research concerned the use of boron trifluoride to remove the water formed in the reaction by the formation of its monohydrate.

The initial nitration of ethyl-N-isopropyl carbamate with an equivalent of fuming nitric acid proved fruitless. The same result was obtained when the nitrating mixture consisted of fuming nitric acid and concentrated sulfuric acid at a slightly elevated temperature.

In those experiments conducted with ethyl-N-isopropyl carbamate, fuming nitric acid and boron trifluoride vigorous oxidation accompanied all the reactions in which there was an attempt to recover the boron trifluoride. When the attempts to recover the boron trifluoride were abandoned, the only successful nitration occurred when the reaction was carried out at 0°C. and then immediately diluted with a large volume of ice water. Although several other procedures; including, neutralization at the conclusion of the reaction, reactions at elevated temperatures (to insure continuous reaction), and variation of the sequence of addition, were investigated; the net result was oxidation. Once decomposition had commenced it was very

exothermic, as evidenced by the fact that the reaction mixture reached a temperature of 120°C. in about a minute when the oxidation was allowed to proceed unimpeded. This extreme susceptibility to oxidation was attributed to the unusually reactive hydrogen on the central carbon of the isopropyl radical.

It was originally believed that the oxidation was merely due to a "reaction lag". This would result in an excess of unreacted acid, which would cause oxidation once the concentration became too large. This explanation was found more satisfactory when the possibility of ionization of the acid in the nitrating mixture at the beginning of the reaction was taken into account. The fuming nitric acid used contained 13% water, which was sufficient to effect such an ionization. The nitrate ion, so produced, is an extremely strong oxidizing agent. The complete lack of oxidation in the experiments with absolute nitric acid well substantiated this reasoning. In these same nitrations with absolute nitric acid it was found that the nitration was five times as great when boron trifluoride was used as when no dehydrating agent was employed.

Since the ethyl-N-isopropyl carbamate was so easily oxidized a few reactions were conducted with the more stable ethyl-N-methyl carbamate. Yields of over 50% were obtained when the carbamate was added to a boron trifluoride -- nitric acid mixture at a temperature below 0°C. There was no oxidation so long as the reaction mixture was kept below 20°C. or immediately diluted with a large volume of water once the reaction had been

completed. Several physical constants of ethyl-N-nitro-N-methyl carbamate were determined: B.P., 73-74°C. at 2.5 mm.;

$n_D^{20} = 1.4480$; $n_D^{23} = 1.4469$; solubility, 1.64 g. per 100 cc. of water at 15°C.

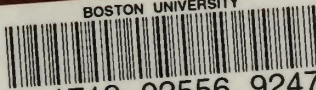
Two methods of dehydration with inorganic salts, sodium bisulfate and anhydrous sodium sulfate, were also investigated. Although some degree of nitration of ethyl-N-isopropyl carbamate was effected, the yields were very small, the maximum being 3%. In those reactions with ethyl-N-methyl carbamate the results were somewhat better. When the nitrating agent was fuming nitric acid and anhydrous sodium sulfate a yield of 35% was obtained.

In conclusion, the results of this investigation indicate that boron trifluoride is of assistance in the nitrations but the difficulty in controlling the majority of the reactions in which it is employed exceeds its usefulness. Also, in general, it was proven that inorganic salts used as dehydrating agents had almost no effect on increasing the extent of nitration. Lastly, it was found that the reactions with ethyl-N-methyl carbamate were more successful than those with ethyl-N-isopropyl carbamate because the former was less subject to oxidation.

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